Claims

1. An oxygen-resistant iron hydrogenase derived from an oxygen sensitive iron hydrogenase by the substitution of one or more amino acid residues within the hydrogen channel of the oxygen-sensitive iron hydrogenase.

2. The oxygen-resistant iron hydrogenase of claim 1 wherein said substitution is made to one or more amino acid residues selected from the group consisting of residues 78, 240, 244, 86, 248, 247, 82, 89, 355, 93 and 252 of HydA1 iron hydrogenase.

3. The oxygen-resistant iron hydrogenase of claim 1 wherein the substituted amino acid which is at a residue within said hydrogen channel has a side chain volume which is larger than the side chain volume of the amino acid at the same residue in said oxygen-sensitive iron hydrogenases.

4. A nucleic acid encoding the oxygen-resistant iron hydrogenase of claim 1.

5. A vector comprising the nucleic acid of claim 4.

6. Host cell transformed with the vector of claim 5.

7. The host cell of claim 6 wherein the host cell is green algae.

8. A process for producing hydrogen in green algae comprising culturing green algae cells transformed with the vector of claim 5 under conditions wherein the nucleic acid encoding said oxygen-resistant iron hydrogenase is expressed.

9. The process of claim 8 wherein said green algae is *Chlanydomonas reinhardtii.*

10. A method for making a nucleic acid encoding an oxygen-resistant iron hydrogenase comprising:

comparing the sequence of a first oxygen-sensitive iron hydrogenase having known amino acid residues that form a hydrogen channel in said first hydrogenase with a second iron hydrogenase to identify residues that form a hydrogen channel in said second hydrogenase, and

forming a nucleic acid encoding a derivative of said iron hydrogenase wherein one or more amino acid residues within said hydrogen channel are modified to reduce the oxygen sensitivity of said second hydrogenase.

11. The method of claim 10 wherein the crystal structure of said first hydrogenase is known and said comparing is by *in silico* homology modeling.

12. The method of claim 10 wherein said first hydrogenase is CpI and said second hydrogenase is HydA1.

13. A process for making a green algae capable of hydrogen production in the presence of oxygen comprising transforming a green algae with the vector of claim 5.

14. A method of making an oxygen-resistant iron-hydrogenase comprising:

determining the diameter of an H_2-channel defined by a set of amino acid residues in an oxygen-sensitive iron hydrogenase by measuring the distance between the side chains of one or more of the amino acid residues of said set to identity one or more diameter determining amino acid residues; and

modifying one or more of said diameter determining residues in said oxygen-sensitive iron hydrogenase to reduce the effective diameter of said H_2-channel to form an oxygen-resistant iron hydrogenase, whereby the diffusion of oxygen within said modified H_2-channel in said oxygen-resistant iron hydrogenase is reduced as compared to the diffusion of oxygen in said H_2-channel of said oxygen-sensitive iron hydrogenase.

15. The method of claim 14, wherein said H_2-channel residues are identified by homology modeling to a known x-ray structure of one or more known hydrogenases.

16. The method of claim 15, wherein substitution at one or more of said diameter determining residues of said H_2-channel is made in the form of an *in silico* molecule wherein the most energentically favorable rotamer for the substituted side chain is used to minimize the energy of at least the H_2-channel of said molecule.

17. The method of claim 16 wherein GROMOS is used to compute said minimized energy of said molecule.

18. The method of claim 16 wherein the diameter of said H_2-channel in said energy minimized molecule is compared to the diameter of said H_2-channel prior to in silico modification as a basis for selection of one or more mutations to be formed in said oxygen-sensitive iron hydrogenase protein.